UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/845,080 | 04/27/2001 | Wendy Naimark | 00-0238 | 1601 |

27774 7590 04/11/2003

MAYER, FORTKORT & WILLIAMS, PC
251 NORTH AVENUE WEST
2ND FLOOR
WESTFIELD, NJ 07090

| EXAMINER |
|---|
| NGUYEN, DAVE TRONG |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1632 | |

DATE MAILED: 04/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/845,080 | Naimark |
| **Examiner** | **Art Unit** |
| Dave Nguyen | 1632 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *Jan 24, 2003*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *1-5, 7-15, 17, and 37-42* is/are pending in the application.

4a) Of the above, claim(s) *4, 5, and 9* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 7, 8, 10-15, 17, and 37-42* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 6, 16, 18-36 have been canceled, claims 1, 2, 4, 7-12, and 17 have been amended, claims 37-42 have been added by the amendment filed January 24, 2003.

Claims 4-5, and 9, directed to non-elected species have been withdrawn from further consideration by the Examiner.

Claims 1-3, 7-8, 10-15, 17, 37-42, to which the following grounds of rejection are applicable, are pending.

Claims 1, 7-17 are objected because the claims embrace non-elected invention (Group III claims readable on the limitation of exposing the claimed suspension to a incompatible condition). The elected invention is the invention that only embraces a method of exposing a suspension comprising a pharmaceutically active agent and microparticles to a structural component that is compatible with said pharmaceutically active agent. Thus, the claims are required to be amended so as to reflect only on the elected invention.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7-8, 10-15, 17, 37, readable on a genus of components belonging to a pharmaceutical article, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates a method of using a polymeric microparticle to increase a pharmaceutical effectiveness of any pharmaceutically agent exposed to any component that is incompatible to the agent, *e.g.,* a component belonging to a pharmaceutical article, that causes a reduction, for example, by at least 5% in pharmaceutical effectiveness upon contacting a pharmaceutical agent, pages 3 and 4 of the specification. With regard to the claimed genus of components as part(s) of a pharmaceutical article, which are incompatible to any pharmaceutical agent, the specification only teach and discloses sufficiently of medical delivery devices composed of metals or certain polymers (poly ether ether ketones, polyimides, exposies, nylons, polycarbonates and glass, page 2 of the specification).

However, it is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or materials and/or components containing unspecified structures of molecules that are essential for the making the methods as broadly claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of "components" which are employed in the context of delivery any pharmaceutical agent in which a pharmaceutical effectiveness of the agent must be increased upon contacting a generic incompatible component.

It is not sufficient to support the present claimed invention directed to unspecified components other than metallic coating deliver device or polymeric coated medical devices, which must exhibit the biological property of causing a reduction in pharmaceutical effectiveness upon contacting a pharmaceutically active material. A disclosure of no more than a polymeric microparticle in combination with a medical delivery device comprising on its surface a metal, certain polymers or a glass as in the instant case, is simply a wish to know the identity of any other components from any other pharmaceutical article that are applicable to the claimed methods at the time the invention was made. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which is not conventional in the art as of applicants effective filing date. Claiming unspecified molecular structures of other components of a pharmaceutical

article that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of components for use within the context of the claimed invention, which must exhibit the contemplated biological functions, *e.g.,* an increase in a pharmaceutical effectiveness of any pharmaceutical active agent upon contacting any incompatible component, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, In view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 1, 7-8, 10-15, 17, 37 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to:

A method of using suitable polymer microparticles to protect a pharmaceutical effectiveness of a pharmaceutically active agent, comprising:

Providing a pharmaceutically acceptable suspension comprising a pharmaceutically active agent and suitable microparticles, wherein said pharmaceutically active agenet and polymer microparticles are commingled within said pharmaceutically acceptable suspension;

Exposing and contacting said pharmaceutically acceptable suspension to a pharmaceutical article selected from the group consisting of a pharmaceutical article comprising a polymer or metal as an incompatible component, and a medical delivery device comprising a

component which is incompatible with said pharmaceutically active agent, wherein said polymer microparticles result in a pharmaceutical effectiveness of the pharmaceutically active agent in the absence of the microparticles.

The specification does not reasonably provide enablement for the presently pending claims encompassing any other combination of microparticles and component(s). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Specifically, since the claimed invention is not supported by a sufficient written description (for possessing of the genus of the materials which are necessary for the practice of the claimed invention), particularly in view of the reasons set forth above, one skilled in the art would not known how to use and make the claimed invention so that it would operate as intended.

Applicant's response (pages 5 and 6) has been considered by the examiner but is not found persuasive for the reasons of record. Applicant mainly asserts that the MPEP guidelines and the court decisions in *Fiers* and *Eli Lilly* are directed to distinct invention and can not be used as evidence to support the lack of written description of the claimed invention. Applicant's assertion is not found persuasive because insofar as the court decisions have been consistent in stating that a genus claim is not patentable if a representative number of species is not adequately supported and/or described by any as-filed specification coupled with the state of the

prior art. While applicant has reduce the present invention to practice of the species as set forth in the enabling embodiments, *e.g.,* see page 4 of the stated office action, such reduction of practice is not sufficient for claims readable to a genus of any other components of any other pharmaceutical article, which other components and/or pharmaceutical article do not find any adequate written support from the as-filed specification.

In addition, applicant asserts on page 8 that it would be a routine matter for one skilled in the art to (a) further conduct tests so as to determine components that are yet to be discovered as being incompatible with a pharmaceutical agent of interest, and (b) to subsequently determine which microparticles would exhibit the claimed properties for any component as set forth in (a). Applicant's assertion is simply an expressed opinion without any factual evidence in order to demonstrate that a further tests and/or experimentation on items (a) and (b) are well-known in the prior art so that its written description is not required from the as-filed specification, and that only a routine matter is employed to practice the full breadth of the claimed invention. A skilled artisan cannot envision the detailed structure of representative number of species unspecified components other than a metallic-based or polymer-based medical delivery device for use within the context of the claimed invention, *e.g.,* an increase in a pharmaceutical effectiveness of any pharmaceutical active agent upon contacting any incompatible component, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, In view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, and 7-8, 10-17, 37-42 readable on:

A method of using suitable polymer microparticles to protect a pharmaceutical effectiveness of a pharmaceutically active agent, comprising:

Providing a pharmaceutically acceptable suspension comprising a pharmaceutically active agent, *e.g.,* drugs, protein, DNA, plasmids, or any biologically active agents known in the prior art, commingled with suitable polymer microparticles, *e.g.,* polystyrene based polymer,

and exposing and contacting said pharmaceutically acceptable suspension to a medical delivery device comprising a stainless steel based metal, wherein said polymer microparticles result in a pharmaceutical effectiveness of the pharmaceutically active agent in the absence of the microparticles,

are rejected under 35 USC 102(e) as being anticipated by, or in the alternative under 35 USC 103(a), as being unpatentable over Pinchuck *et al.* (US 2002/0107330).

Pinchuk *et al.* teach a medical device, *e.g.,* catheters, guide wires, stents, stent grafts, and a coating over at least a portion or the entirety of the medical device, the coating comprising a biocompatible block copolymer which further comprises polystyrene based polymers, *e.g.,* page 1, paragraphs 0010-0016, page 2, par. 0019-0022, column 2, p. 2, par. 0037, p. 3, par 0040. The teaching of a suspension comprising the block copolymers and a therapeutic agent, wherein the copolymers and therapeutic agents are both present or commingled in a buffered solution before being exposed to a medical device, is clearly taught on page 9, paragraph 0190, and paragraph 0196. Pinchuck also teaches that the microparticles are provided in an amount of an exemplified 1 wt%, *e.g.,* p. 4, par. 0059, page 8, pars 0176-0178, page 11, example 2. The dimensions of the polymeric coating of from about 0.5 microns to 50 microns are disclosed on page 9, par. 0195. Metallic based medical devices are disclosed on page 8, par. 0180. Adenoviral vectors as therapeutic agents are disclosed on page 5, paragraph 0089.

Absent evidence to the contrary and give all of the limitations are met by the disclosure of Pinchuck *et al.,* the claims are clearly anticipated by, or in the alternative, rendered *prima facie* obvious by Pinchuck *et al.*

Applicant asserts on pages 9 and 10 that Pinchuk does not appear to disclosed the newly added limitation, *e.g.,* a solution containing a pharmaceutically active agent and polymer

microparticles combined or commingled in the solution. However, it is apparent that on on page 9, paragraph 0190, and paragraph 0196, Pinchuk teaches the same by providing an example disclosing a solution comprising the block copolymers and a therapeutic agent (paclitaxel) wherein the copolymers and therapeutic agents are both present or commingled in a buffered solution before being exposed to a medical delivery device. Applicant further argued about functional limitations, however, given that the cited reference teach all of the structural limitations and active steps, the polymeric microparticles of the cited reference would necessarily protect and enhance the effectiveness of the delivered biologically active agent, particularly given the absence of evidence to the contrary.

Claims 1, 2, 7, 9-15, 17, 37-42 readable on:

A method of using suitable polymer microparticles to protect a pharmaceutical effectiveness of a pharmaceutically active agent, comprising:

Providing a pharmaceutically acceptable suspension comprising a pharmaceutically active agent, *e.g.,* drugs, protein, DNA, plasmids, or any biologically active agents known in the prior art, commingled with suitable polymer microparticles, *e.g.,* polystyrene based polymer, and a metal compound, *e.g.,* any metal compound including those metal compounds that form basic components of a metallic medical delivery device,

wherein said polymer microparticles result in a pharmaceutical effectiveness of the pharmaceutically active agent in the absence of the microparticles,

Are rejected under 35 USC 102(e) as being anticipated by Mathiowitz (US 6,248,720).

Mathiowitz teaches the identical method on Table 1, column 11, column 13, lines 21-45, column 14, lines 33-49, column 23, and Example 2. Size and concentration of polymeric microparticles are disclosed on columns 7 and 8. Blends of polystyrene based microparticles are disclosed on column 11, line 50.

Absent evidence to the contrary and give all of the limitations are met by the disclosure of the recited reference, the disclosed microparticles as employed in the delivery method of

Mathiowitz would enhance the pharmaceutical effectiveness of the delivered agent such as drugs and/or DNA in the absence of the microparticles.

Claims 1-3, 7-8, 10-15, 17, 37-42 readable on

A method of using suitable polymer microparticles to protect a pharmaceutical effectiveness of a pharmaceutically active agent, comprising:

Providing a pharmaceutically acceptable suspension comprising a pharmaceutically active agent, *e.g.,* drugs, protein, DNA, plasmids, or any biologically active agents known in the prior art, commingled with suitable polymer microparticles, *e.g.,* polystyrene based polymer,

and exposing and contacting said pharmaceutically acceptable suspension to a medical delivery device comprising a stainless steel based metal, wherein said polymer microparticles result in a pharmaceutical effectiveness of the pharmaceutically active agent in the absence of the microparticles,

are rejected under 35 USC 103(a) as being unpatentable over Mathiowitz taken with Barry (WO 01/30403) or Pinchuk *et al.* (US 20002/0107330 A1).

The rejection of the base claims is applied here as indicated above. To the extent that Mathiowitz does not teach that a metallic or polymer coated medical delivery device is employed to deliver the biologically active agent encapsulated controlled release polymeric microparticles, Both Barry and Pinchuk (entire disclosure) teach that it is well-established in the prior art that medical delivery devices including those of metallic based catheter and/or polymer coated metallic based catheters are routinely employed for delivery of biologically active agent to any desired cell *in vivo.*

It would have been obvious for one of ordinary skill in the art to employ any medical delivery device available in the prior art including those described in the cited references to deliver the encapsulated active agents of Mathiowitz to a target cell *in vivo.* One of ordinary skill in the art of controlled released carriers and medical techniques would have been motivated to employ the medical devices of Barry and Pinchuk because both Barry and Pinchuk teach that it

is well-established in the prior art that medical delivery devices including those of metallic based catheter and/or polymer coated metallic based catheters are routinely employed for delivery of biologically active agent to any desired cell *in vivo,* and teach the advantages of employed their medical delivery devices as a medical tool to deliver any biologically active agent to a cell.

Thus, the claimed invention, as a whole, was *prima facie,* obvious.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **(703) 305-2024**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Deborah Reynolds*, may be reached at **(703) 305-4051.**

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is **(703) 305-7401**.

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Trong Nguyen
Primary Examiner
Art Unit: 1632

DAVE T. NGUYEN
PRIMARY EXAMINER